



J. SAFRA SARASIN
— SUSTAINABLE ASSET MANAGEMENT —



Thematic Insights: Future Health Gene Sequencing: Hacking the Code of Life

J. Safra Sarasin Sustainable Asset Management
Q4/2021

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Commentary from the Portfolio Management Team

Volatile Q4 equity market

The volatile but overall positive equity market environment continued in Q4 2021. However, the emergence of a new COVID-19 variant called Omicron caused a negative market reaction. Early health data shows that Omicron is spreading much faster than the previously dominating Delta variant. While infection rates are rising extremely fast the hospitalisation and mortality rates remain lower than in previous COVID-19 waves.

In addition, the Fed signaled in November that inflation is more persistent than initially anticipated and it sees inflation not only as a transitory phenomenon. In an effort to rein in the price increases, US policy makers are now planning three interest rate hikes in 2022. Consequently, investors rotated away from expensive and non-earnings generating growth stocks, including small & mid-cap biotech and healthcare technology firms, into lower valued cyclical health care services or defensive pharma companies.

Good earnings season

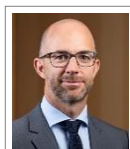
The fund delivered a +3.3% (P USD acc) return in Q4 2021. While it outperformed the average peer health fund it substantially lagged the overall equity market in Q4. The portfolio remained resilient and in positive absolute territory thanks to solid Q3 earnings results in general and outstanding results of our holdings including Vocera, Nike and Essilor. The most negative investor reactions were triggered by companies which are earnings negative and are stepping up additional investments like Phreesia, Teladoc and Exact Science. While the mid to long-term market opportunities of these disruptive companies remain bright, investors are currently dumping these type of growth stocks.

Last quarter we initiated one new portfolio position. We bought Teleflex, a mid-sized, diversified US Medtech company, at an attractive entry price. The company has suffered over the last quarters from COVID-19 restricted patient access to urologist practices. Its innovative Urolift product line didn't meet short term investor expectations. We expect a fast recovery post this Omicron wave.

Gene sequencing – hacking the code of life

Life on Planet Earth is encoded in either DNA or RNA. DNA is a simple code of four molecules that acts as a blue print. Reading this code helps us to understand how we are made, how we are related, how errors or mutations in our DNA cause diseases and which drugs are most appropriate to treat them. Reading and writing this code is driving a revolution and creating new industries. The first human genome “read” was completed in 2001, took 10 years, and cost USD 3bn. Since 2005, a technique termed Next Generation Sequencing (NGS) has driven down the cost per human genome to around USD 600 (with the target being USD 100 in the near future), and sped up the process to less than one day. The current USD 6bn market from NGS predominantly comes from sales for research purposes and identification of rare genetic diseases, but a rapidly increasing clinical oncology market has developed. Tumors are often now defined and treated based on the mutations found in the cancer cells, rather than just the location on the body. The NGS instrument market is dominated by Illumina, with Pacific Bio and Oxford Nanopore (ONT) more recent entrants with differentiated technology.

Source: Bank J. Safra Sarasin Ltd, as of 31.12.2021. Past performance is no indicator or guarantee for future performance. Company examples do not constitute a request or offer, solicitation or recommendation to buy or sell investments or other specific financial instruments, products or services.



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The barriers to entry in this market are significant, with many well-resourced healthcare companies having attempted to enter and failed. While the potential total addressable market (PTAM) for traditional short-read NGS is large, there are limitations to the technique. The process involves reading short fragments of DNA at a time, then sticking them back together using computer software, which leaves many gaps or uncertainties in the output. An alternative technique, termed “long-read”, reads thousands of bases in a single continuous read and may help to expand the TAM for NGS. ONT uses long-read and nanopores to miniaturize the process (even conducting DNA analysis in the International Space Station), and give rapid real-time results. It employs a razor/razor blade business model, i.e. instrument placements driving sales of consumables, and it is rapidly growing.

Our ability to understand and treat complex diseases has been limited with existing technologies, but studies using ONT's long-read NGS technology are underway to tackle even the most complex of diseases (for example, Alzheimer's disease).

One interesting emerging use of NGS is for early cancer detection through liquid biopsies (blood-test to detect cancer; covered in a previous Thematic Insight). Indeed, driven by monitoring, therapy selection, and screening, the NGS oncology market is the largest near-term opportunity, in our view. Along with the fight against cancer, NGS is important in the fight against COVID-19, being used to detect variants (reading RNA). Further forward, NGS could be used in immunoprofiling, microbiome testing (in diary market, for example), agriculture, and environmental testing. Along with reading DNA with NGS, companies like Twist Bioscience in a field called Synbio (Synthetic Biology) are writing DNA to produce new drugs, enzymes, biofuel, data storage, and much more.

We think NGS and DNA writing are likely to disrupt several industries, but with the biggest near-term leap forward in healthcare. It's not science fiction to imagine sequencing at birth, and regular blood tests for any cancer, becoming standard practice within the next decade. Overall, we see the market as highly attractive and we expect a long runway for growth. In combination, the potential markets could create a potential TAM in the multiple of USD 100's bn.

Learn more about

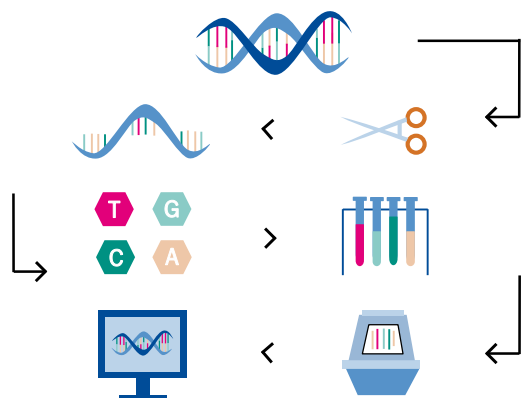
Gene Sequencing : Hacking the Code of Life in our thematic insights on the next page.


Next-Generation Sequencing: Hacking the Code of Life



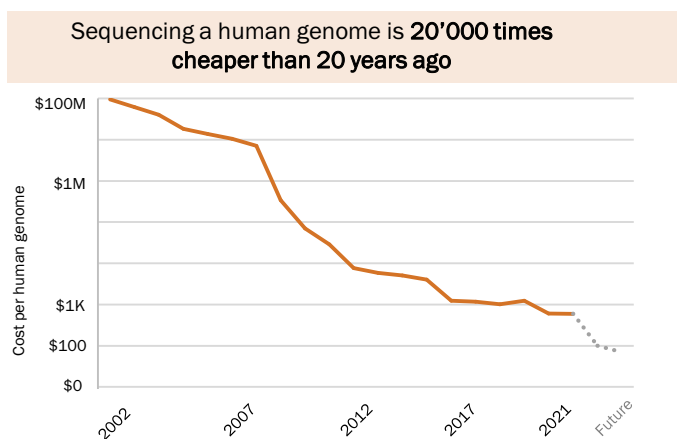
Reading our DNA is essential to understanding how we are made, how mutations cause diseases, and how we respond to drugs. Steady progress has allowed us to read the code faster and at a fraction of the cost. Beyond current uses for research, population genetics and diagnosing genetic diseases, we see many further exciting applications emerging for NGS. The NGS oncology market is the largest near-term opportunity with a potential total addressable market (PTAM) of >\$150B. Along with the fight against cancer, NGS is used to detect COVID-19 variants within an infectious disease market that has a >\$65B PTAM. Future applications will go beyond healthcare and could result in market opportunities greater than \$300B per year. Hacking the code of life will move the world forward and be lucrative for the companies involved.


Next- Generation Sequencing (NGS): What it is



 NGS is crucial to unlock information held in our genome to better understand our genetic makeup

Decreasing Costs and improving speed of results

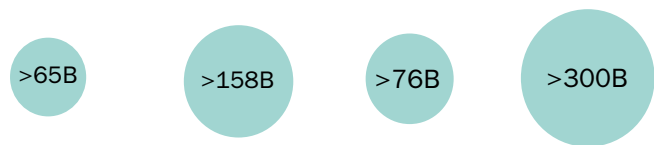


 Today, we are able to **sequence an entire human genome**, all 3.2 billion letters, in a matter of hours







NGS: Emerging Applications in Growing Markets

Near-term	Timeline to Market Disruption		Long-term
Infectious diseases	Cancer	Autoimmune disorder	Future Applications
Diagnose variants faster and with more sensitivity	Identify and treat markers with greater precision	Discover genomic mutations	Includes: Synbio Gene editing Liquid biopsy

Potential Total Addressable Market (in USD):



Case study : Investing in the NSG Value Chain

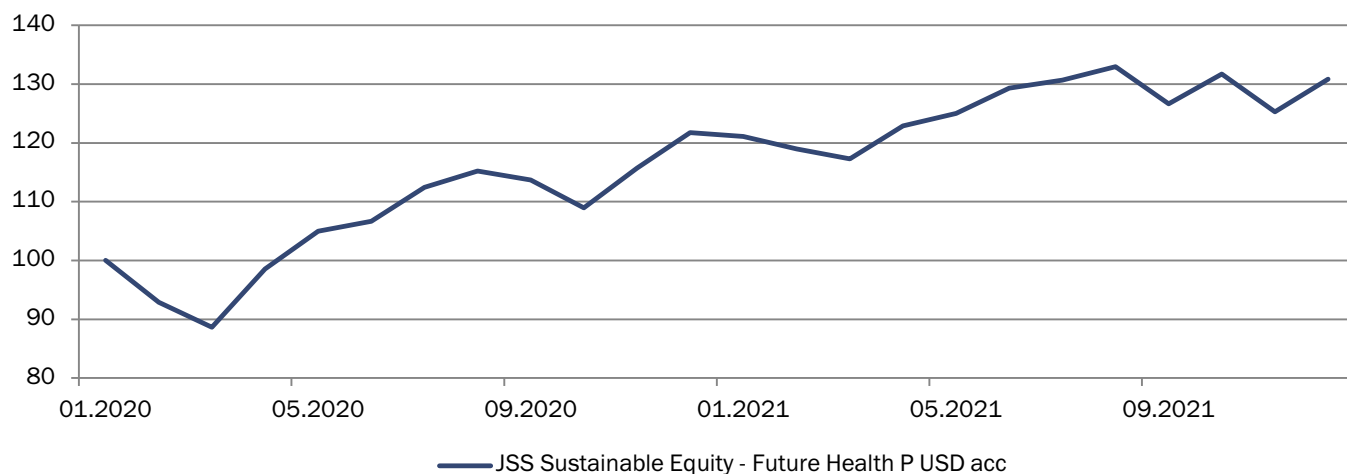
	Preparation Extraction kits and tests Medium barriers to entry	
	Sequencing Platforms Desktop machines High barriers to entry	
	Data Computing High computing chips for data interpretation and storage High barriers to entry	

Sources: ¹ National Human Genome Research Institute, Data: DNA Sequencing Costs, December 2021; ² DeciBio, Market Research: Health Advances, December 2021.

The companies presented are provided as example investments and might not be part of the investment portfolio of the fund. The examples are given for illustrative purposes only and do not account for individual circumstances of potential investors.

Performance Report

Historical net performance since inception (in USD; 21.01.2020 – 31.12.2021)

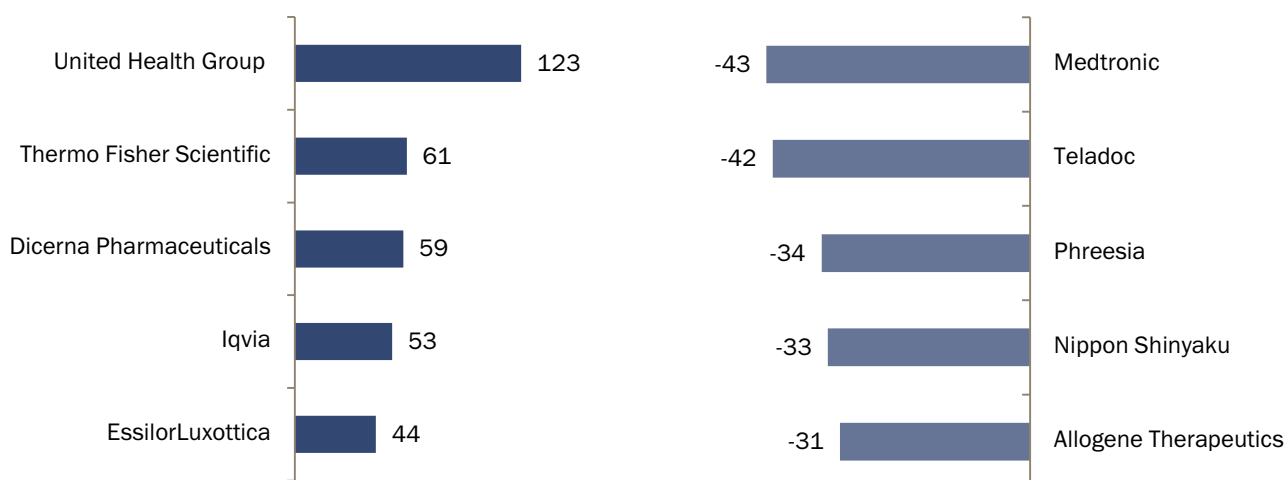


Monthly net performance since inception in % (P USD acc)

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Year
2021	-0.58%	-1.75%	-1.42%	4.78%	1.73%	3.45%	1.05%	1.76%	-4.75%	4.00%	-4.88%	4.42%	7.4%
2020	-3.36%*	-7.13%	-4.57%	11.19%	6.55%	1.61%	5.39%	2.48%	-1.35%	-4.14%	6.17%	5.25%	18.09%

*share class launched 21.01.2020

Top 5 and bottom 5 contributors to return (Period: 01.10.2021 – 31.12.2021, in bps)



Source: Bank J. Safra Sarasin Ltd, Datastream, Bloomberg, as of 31.12.2021. Past performance is no indicator or guarantee for future performance.

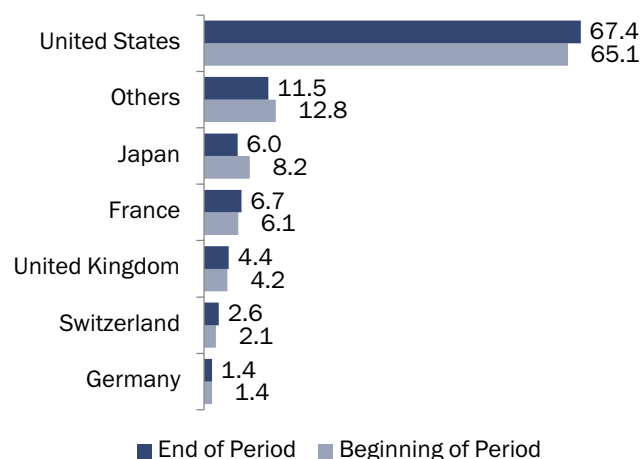
Allocations Report

Top 10 holdings (as of 31.12.2021)

Security	Country	Sector	Theme	Weight (%)
United Health Group	United States	Health Care	Infrastructure & Technology	5.4%
EssilorLuxottica	France	Consumer Discretionary	Prevention & Diagnostics	4.5%
AstraZeneca	United Kingdom	Health Care	Treatment	4.4%
Thermo Fisher Scientific	United States	Health Care	Prevention & Diagnostics	4.1%
Johnson & Johnson	United States	Health Care	Treatment	3.6%
Iqvia	United States	Health Carre	Prevention & Diagnostics	3.4%
Danaher	United States	Health Care	Prevention & Diagnostics	3.2%
Edwards Lifesciences	United States	Health Care	Treatment	2.9%
Kerry Group	Ireland	Consumer Staples	Prevention & Diagnostics	2.8%
Novo Nordisk	Denmark	Health Care	Treatment	2.7%
Total				37.1%

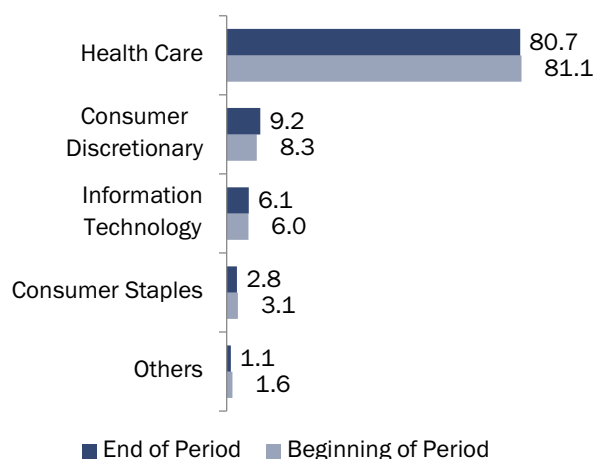
Geographical allocation in %

(Period: 01.10.2021 – 31.12.2021)



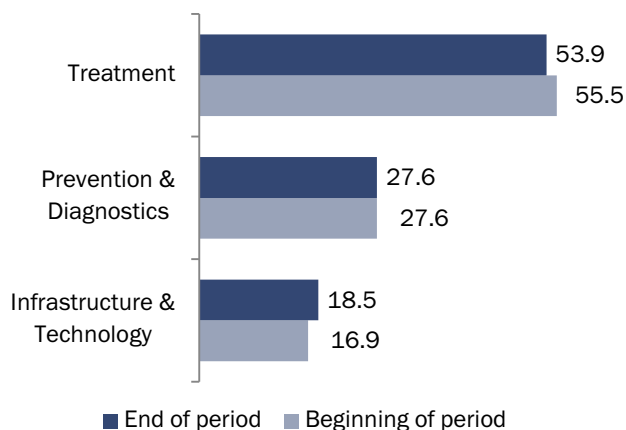
Sector allocation in %

(Period: 01.10.2021 – 31.12.2021)



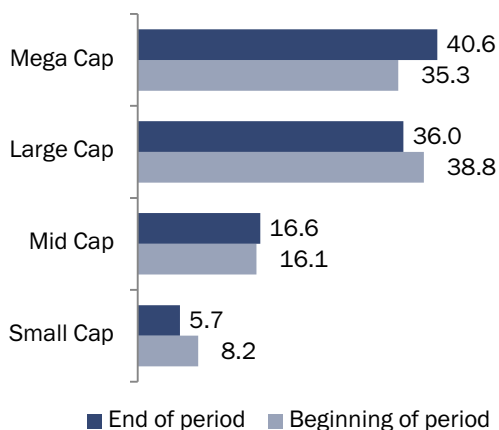
Thematic allocation in %

(Period: 01.10.2021 – 31.12.2021)



Size allocation in %

(Period: 01.10.2021 – 31.12.2021)



Source: Bank J. Safra Sarasin Ltd, Datastream, Bloomberg, as of 31.12.2021. Allocations may change without notice.

Pictures from Gettyimages, otherwise specified.

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